REMARKS

Claim 13, as amended, and claims 14-17 are pending in the instant application. No new matter has been added as a result of the above-described amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

1. Rejection of claims 13-17 under 35 U.S.C. § 112, second paragraph

The Office Action maintains a rejection of claims 13-17 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. The Action states that it is unclear whether the negative proviso "but not the extracellular region of TACI (SEQ ID NO: 15) or the extracellular region of BCMA (SEQ ID NO: 6)" in claim 13 is to be applied to i and ii in addition to iii, or is exclusive to iii.

Applicants contend that one of ordinary skill in the art would understand that the portion of claim 13 beginning with "P^1, P^2, P^3, and P^4 are each independently" and ending with the proviso "but not the extracellular region of TACI (SEQ ID NO: 15) or the extracellular region of BCMA (SEQ ID NO: 6)" means that any one of P^1, P^2, P^3, and P^4 can be the consensus region of TACI (SEQ ID NO: 16), the consensus region of BCMA (SEQ ID NO: 7), or the TACI/BCMA extracellular consensus sequence (SEQ ID NO: 13), and that any one of P^1, P^2, P^3, and P^4 cannot be the extracellular region of TACI (SEQ ID NO: 15) or the extracellular region of BCMA (SEQ ID NO: 6). Applicants, therefore, contend that claim 13 is not indefinite. However, in order to more particularly point out and distinctly claim the subject matter that Applicants regard as the invention, and in Applicants' view because it will have no substantive effect on the proper scope of the pending claims, Applicants have amended claim 13 to recite that "P^1, P^2, P^3, and P^4 are not the extracellular region of TACI (SEQ ID NO: 15) or the extracellular region of BCMA (SEQ ID NO: 6)." Applicants contend that claim 13, as amended, is not indefinite and respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

2. Rejection of claims 13-15 under 35 U.S.C. § 112, first paragraph

The Office Action maintains a rejection of claims 13-15 under 35 U.S.C. § 112, first

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300 South Wacker Drive
Chicago, Illinois 60606
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paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants' understanding of this rejection is fully set forth in Applicants' response to the Office Action mailed December 1, 2004.

Applicants respectfully disagree with the Action's assertion that the specification does not contain an adequate written description of the claimed invention. Applicants note that the *Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, P1, "Written Description" Requirement* ("*Guidelines*") state that an adequate written description of the claimed invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Guidelines,* 66 Fed. Reg. 1099, 1105 (2001). With regard to a claim directed to a genus, the *Guidelines* specifically state that the written description requirement may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or reduction to drawings, or by disclosure of relevant, identifying characteristics (*i.e.*, structure or other physical or chemical properties, or by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics) sufficient to show the applicant was in possession of the claimed genus. *Guidelines,* 66 Fed. Reg. 1099, 1106 (2001).

The Action states that the specification does not disclose a representative number of species within the claimed genus of the composition. The *Guidelines*, however, clearly state that a description of a representative number of species is but one way in which the written description requirement can be satisfied. *Id.* In the instant case, the written description requirement has been satisfied by the disclosure in the specification of relevant, identifying characteristics of the molecules encompassed by claimed genus, and therefore, whether or not the specification discloses a representative number of species within the claimed genus is irrelevant.

The Action also states that claims 13-15 do not limit the functional attributes of the encompassed molecules, and that one of ordinary skill in the art would reasonably conclude that claims 13-15 are not limited to binding AGP-3 or APRIL. According to the *Guidelines*, however, claims 13-15 need not contain an explicit functional limitation in order to satisfy the written

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300 South Wacker Drive
Chicago, Illinois 60606
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description requirement. Rather, the written description requirement may be satisfied by a disclosure of relevant, identifying characteristics of the molecules encompassed by claimed genus (*e.g.*, functional characteristics coupled with a known or disclosed correlation between function and structure). In the instant case, the specification *explicitly discloses* that (a) TACI and BCMA are cell-surface receptors for APRIL (page 60, lines 14-19); (b) APRIL competes with AGP-3 for TACI and BMCA binding (page 60, lines 15-18); (c) soluble BMCA competes with APRIL and AGP-3 for receptor binding, ameliorating T cell-dependent and T cell-independent humoral immune responses *in vivo* (page 5, lines 7-10; page 60, lines 25-27); and (d) soluble TACI competes with APRIL and AGP-3 for receptor binding, ameliorating T cell-dependent and T cell-independent humoral immune responses *in vivo* (page 5, lines 10-12; page 60, lines 24-27). The specification also *explicitly discloses* molecules such as those recited in claims 13-16, comprising at least one specific binding partner, wherein a "specific binding partner" is a molecule that preferentially binds to a protein of interest (*e.g.*, TACI and BCMA), including molecules such as solublized receptors (*e.g.*, soluble TACI and soluble BCMA) (page 13, lines 14-19; page 32, line 22 to page 33, line 18). The specification also *explicitly discloses* that soluble receptor fragments such as the consensus region of TACI (SEQ ID NO: 16), the consensus region of BCMA (SEQ ID NO: 7), and the TACI/BCMA extracellular consensus sequence (SEQ ID NO: 13) constitute specific binding partners (page 33, line 24 to page 34, line 3). Thus, the specification's teachings clearly show that disease states associated with APRIL and AGP-3 activity can be modulated using TACI, BCMA, APRIL, or AGP-3, or portions thereof, either individually or in combination (page 5, lines 19-27).

Applicants contend that because the specification *explicitly discloses* relevant, identifying characteristics of the molecules encompassed by claimed genus (*i.e.*, functional characteristics coupled with a known or disclosed correlation between function and structure), and because the claims are limited to molecules comprising at least one of three specific binding partners that are *explicitly disclosed* in the specification (*i.e.*, the consensus region of TACI, the consensus region of BCMA, and the TACI/BCMA extracellular consensus sequence), the specification contains an adequate written description of the claimed invention. Applicants, therefore, respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

McDonnell Boehnen Hulbert & Berghoff LLP
300 South Wacker Drive
Chicago, Illinois 60606
312-913-0001

3. Rejections of claims 13-15 under 35 U.S.C. § 103(a)

The Office Action maintains a rejection of claims 13-15 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 98/39361 (the '361 publication) in view of International Publication No. WO 99/11791 (the '791 publication). The Office Action also maintains a rejection of claims 13-15 under 35 U.S.C. § 103(a), as being unpatentable over U.S. Patent No. 6,475,987 (the '987 patent) in view of the '791 publication. Applicants' understanding of these rejections are fully set forth in Applicants' response to the Office Action mailed December 1, 2004.

Applicants note that an analysis of obviousness must be based on the following factual inquiries: (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the art at the time the invention was made; and (4) objective evidence of nonobviosuness, if any. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966). Moreover, where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 *also requires* consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). As the Federal Circuit has emphasized: "[b]oth the suggestion and the reasonable expectation of success must be founded in the prior art, not the Applicants' disclosure." *Id.* Applicants contend that because neither the suggestion to make the claimed composition nor the reasonable expectation of success can be found in the combinations cited in the Action, the rejections based on 35 U.S.C. § 103(a) should be withdrawn.

Applicants respectfully disagree with the Action's assertion that either the '361 and '791 publications in combination or the '987 patent and the '791 publication in combination render the claimed invention obvious. In particular, Applicants contend that these combinations not only fail to suggest that one of ordinary skill in the art should make the claimed composition, but instead teach away from the claimed composition. While the '791 publication may teach – as the Action asserts – that the cysteine-rich pseudo-repeats in the extracellular domains of TNF receptor superfamily members are *involved* in ligand binding (page 7, lines 24-29), the '791 publication does *not* teach that

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300 South Wacker Drive
Chicago, Illinois 60606
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the cysteine-rich pseudo-repeats are *sufficient* for ligand binding. Quite to the contrary, when the '791 publication refers to the ligand binding domain, it refers to the *entire* extracellular domain (*see* page 1, lines 22-23; page 9, lines 15-17; page 29, lines 22-23; page 69, line 30; page 78, line 18; and page 121, line 24) – with the cysteine-rich pseudo-repeats merely constituting a component of the ligand binding domain (*see, e.g.*, page 18, lines 4-6; page 106, lines 14-16). For example, the '791 publication states that:

> In one embodiment, the invention provides a soluble active fragment of an AP04 polypeptide. Such *a soluble active fragment includes the ligand binding domain* of an AP04 polypeptide *and can be*, for example, *a truncated polypeptide encoding the extracellular domain* of an AP04 polypeptide.

(page 25, lines 6-11) (emphasis added). The '791 publication also states that:

> In one embodiment, the invention provides *a soluble AP06 active fragment that includes an AP06 ligand binding domain*. A soluble AP06 active fragment *can be*, for example, *a truncated polypeptide encoding the extracellular domain* of an AP06 polypeptide.

(page 29, lines 7-11) (emphasis added). The '791 publication, however, never states that the cysteine-rich pseudo-repeats *alone* constitute the "ligand binding domain" or an embodiment of the "soluble active fragment" of the invention.

More telling, however, is the fact that while none of the '791 publication's 43 claims recite a ligand binding active fragment comprising only the cysteine-rich pseudo-repeats of the extracellular domain (despite the fact that there is no surcharge for inclusion of additional claims in International applications), claim 9 recites an "active fragment [that] is an AP04 extracellular ligand binding domain." Clearly, even the applicant of the '791 publication did not recognize that the cysteine-rich pseudo-repeats alone are sufficient for ligand binding. In view of the teachings of the '791 publication, one of ordinary skill in the art would understand that the *entire* extracellular domain with its cysteine-rich pseudo-repeats – and not merely the cysteine-rich pseudo-repeats – is necessary for ligand binding. Because the '791 publication simply does not equate the cysteine-rich pseudo-repeats with ligand binding, one of ordinary skill in the art would not have been motivated, *without* considering Applicants' disclosure, to substitute a polypeptide comprising residues 33-104 for the complete extracellular domain in the fusion proteins disclosed in the '361 publication or to substitute a polypeptide comprising the cysteine-rich repeat of the BCMA extracellular domain in the fusion

McDonnell Boehnen Hulbert & Berghoff LLP
300 South Wacker Drive
Chicago, Illinois 60606
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protein comprising the immunoglobulin Fc domain disclosed in the '987 patent. Applicants respectfully contend that rejections based on 35 U.S.C. § 103(a) have been traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Canella believes it to be helpful, she is invited to contact the undersigned representative by telephone at 312-913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

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By: _____
Donald L. Zuhn, Jr., Ph.D.
Reg. No. 48,710

McDonnell Boehnen Hulbert & Berghoff LLP
300 South Wacker Drive
Chicago, Illinois 60606
312-913-0001